(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 March 2001 (01.03.2001)

PCT

(10) International Publication Number
WO 01/14395 A3

(51) International Patent Classification[7]: C07H 15/04, A61K 31/70, A61P 35/00

(21) International Application Number: PCT/US00/22894

(22) International Filing Date: 18 August 2000 (18.08.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/150,088 20 August 1999 (20.08.1999) US

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(81) Designated States *(national)*: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
7 September 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/14395 A3

(54) Title: NOVEL GLYCOCONJUGATES, GLYCOAMINO, ACIDS, INTERMEDIATES THERETO, AND USES THEREOF

(57) Abstract: The present invention provides novel n-alkenyl glycosides and glycoconjugates, n-alkyl glycoamino acids, and methods for the synthesis thereof. In another aspect, the present invention provides novel clustered glycopeptides and methods for the synthesis thereof. In still another aspect, the present invention provides methods for the treatment of cancer, preferably for the prevention of recurrence of cancer, and methods for inducing antibodies in a subject, comprising administering to a subject in need, an effective amount of any of the inventive glycoconjugates as disclosed herein.

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 00/22894

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07H15/04 A61K31/70 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07H A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 96 34005 A (SLOAN KETTERING INST CANCER) 31 October 1996 (1996-10-31) claims --- S. F. SLOVIN ET AL.: "Carbohydrate vaccines in cancer: Immunogenicity of a fully synthetic globo H hexasaccharide conjugate in man" PROC. NATL. ACAD. SCI. USA, vol. 96, 1999, pages 5710-5715, XP002155262 the whole document --- -/--	1,2,11, 13,39-55
X		1,2,11, 13,33, 34,36, 38-55

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 December 2000	10. 04 2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040. Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	de Nooy, A

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	RAGUPATHI, GOVINDASWAMI ET AL: "Immunization of mice with a fully synthetic globo H antigen results in antibodies against human cancer cells: a combined chemical-immunological approach to the fashioning of an anticancer vaccine" ANGEW. CHEM., INT. ED. ENGL. (1997), 36(1/2), 125-128, XP002155263 cited in the application the whole document ---	1,2,11, 13,33, 34,36, 38-55
X	RAGUPATHI, GOVINDASWAMI ET AL: "A fully synthetic globo H carbohydrate vaccine induces a focused humoral response in prostate cancer patients: a proof of principle" ANGEW. CHEM., INT. ED. (1999), 38(4), 563-566, XP002155264 the whole document ---	1,2,11, 13,33, 34,36, 38-55
X	PARK, TAE KYO ET AL: "Total Synthesis and Proof of Structure of a Human Breast Tumor (Globo-H) Antigen" J. AM. CHEM. SOC. (1996), 118(46), 11488-11500, XP002155265 cited in the application page 11494, structure 64 ---	1,2,11, 13
A	LASSALETTA, JOSE ET AL: "Glycosyl imidates. Part 75. Synthesis of the hexasaccharide moiety of globo H (human breast cancer) antigen" LIEBIGS ANN. (1996), (9), 1417-1423, XP002155266 page 1417, structure 1b ---	1
A	B. FRASER-REID ET AL.: "n-Pentenyl glycosides in organic chemistry: A contemporary example of serendipity" SYNLETT, 1992, pages 927-942, XP002155267 cited in the application page 932, scheme 6 page 933, reaction compounds 37,51,52 page 937, reaction compounds 83-86 page 938, scheme 11 --- -/--	4,14

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 00/22894

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	U. E. UDODONG ET AL.: "A ready, convergent synthesis of the heptasaccharide GPI membrane anchor of rat brain Thy-1 glycoprotein" J. AM. CHEM. SOC., vol. 115, 1993, pages 7886-7887, XP002155268 cited in the application page 7887, scheme III	4,14
A	D. CABARET, M. WAKSELMAN: "Amphiphilic liposaccharides. Synthesis and reductive cleavage of C-allyl, O-allyl, and O-butenyl glycosyl derivatives" CARBOHYDRATE RESEARCH, vol. 189, 1989, pages 341-348, XP002155269 page 341, compounds 11 and 12	3
A	C. BAYLE ET AL.: "O-(3-Butenyl), a stable blocking group removable by ozonolysis" CARBOHYDRATE RESEARCH, vol. 232, 1992, pages 375-380, XP002155270 page 376, compounds 1 and 2	3
A	WO 98 46246 A (HINTERMANN SAMUEL ;LIVINGSTON PHILIP O (US); SLOAN KETTERING INST) 22 October 1998 (1998-10-22) figures 18-21	27
A	BRODDEFALK J ET AL: "Preparation of a Glycopeptide Analogue of Type II Collagen -- Use of Acid Labile Protective Groups for Carbohydrate Moieties in Solid Phase Synthesis of O-Linked Glycopeptides" TETRAHEDRON LETTERS,NL,ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 37, no. 17, 22 April 1996 (1996-04-22), pages 3011-3014, XP004029705 ISSN: 0040-4039 page 3011, structure 1	27
P,X	ALLEN, JENNIFER R. ET AL: "A second generation synthesis of the MBr1 (Globo-H) breast tumor antigen: new application of the n-pentenyl glycoside method for achieving complex carbohydrate protein linkages" CHEM.--EUR. J. (2000), 6(8), 1366-1375, XP002155271 the whole document	1,2,4, 11,13, 14,16, 33-36, 38-55

2

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

rnational application No.
PCT/US 00/22894

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 40-55 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see PCT/ISA/ extra sheet

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-14 (in part), 17 (in part), 21-28 (in part), 33-35 (in part), 39-55 (in part)

Present claims 1-14, 17, 21-28, 33-35, 39-55 relate to an extremely large number of possible compounds/products/methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds/products/methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/products/methods in which A of the first structure of claim 1 is chosen from the possibilities of claim 11, that is, A is restricted to be: Globo-H, fucosyl GM1, KH-1, glycophorin, N3, Tn, TF, STN, (2,3)ST, 2,6-STn, and Ley; and R of the first structure of claim 1 is chosen from: allyl, -CH2CH(CO2R')(NHR''), wherein R' or R'' are each independently hydrogen, protecting group, substituted or unsubstituted alkyl, a linker, aryl, peptide, protein or lipid; or NHR''', wherein R''' is a protein, peptide, or lipid linked to N directly or through a crosslinker.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-11 (in part), 13 (in full), 14 (in part), 16 (in full), 17-18 (in part), 20 (in full), 21-36 (in part), 38 (in full), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is Globo H and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

2. Claims: 1-11 (in part), 12 (in full), 14 (in part), 15 (in full), 17-18 (in part), 19 (in full), 21-36 (in part), 37 (in full), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is fucosyl GM1 and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

3. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is KH-1 and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

4. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is glycophorin and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

5. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is N3 and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

6. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is Tn and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

7. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is TF and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

8. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is STN and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

9. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is (2,3)ST and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

10. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the first structural formula of claim 1 where A is 2,6-STn and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

11. Claims: 1-11 (in part), 14 (in part), 17-18 (in part), 21-36 (in part), 39-55 (in part)

Compounds, methods of synthesis and uses related to the

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

first structural formula of claim 1 where A is Ley and R is as defined in claim 1 (as limited according to article 17(2)(a) PCT).

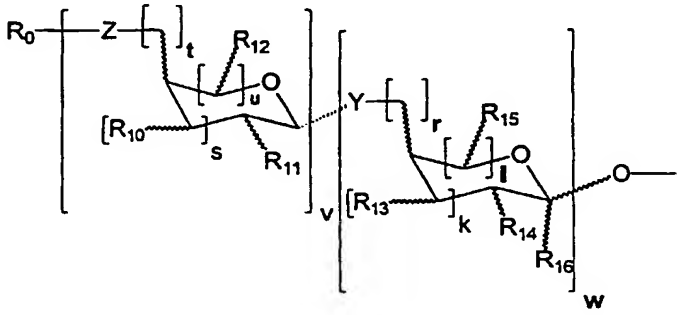
INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/22894

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9634005 A	31-10-1996	US	5708163 A	13-01-1998
		AU	716699 B	02-03-2000
		AU	5672196 A	18-11-1996
		CA	2218884 A	31-10-1996
		EP	0823913 A	18-02-1998
		JP	11504337 T	20-04-1999
		US	5679769 A	21-10-1997
		US	6090789 A	18-07-2000
WO 9846246 A	22-10-1998	AU	6779298 A	11-11-1998
		EP	0996455 A	03-05-2000

hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; wherein R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, OH, OR^{iii}, NH_2, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group; and wherein R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group, with the proviso that if A is KH-1, N3, Globo-H, glycophorin, Tn, TF, STN, (2,3)ST, 2,6-STn or Le^y, and A is α-O-linked, then n is at least 1.

2. The compound of claim 1, wherein R is allyl.

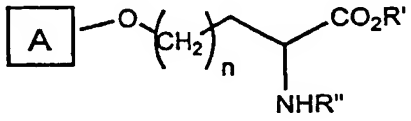
3. The compound of claim 1, wherein n is 1 and R is allyl.

4. The compound of claim 1, wherein n is 2, and R is allyl.

5. The compound of claim 1, wherein R is NHR'", and wherein the protein R'" is KLH or Bovine Serine Albumin, whereby said compound is a glycoconjugate.

6. The compound of claim 1, wherein R is NHR'", and wherein the lipid R'" is PamCys, whereby said compound is a glycoconjugate.

7. The compound of claim 1, wherein R is $CH_2CH(CO_2R')(NHR")$ and the resulting glycopeptide has the structure:



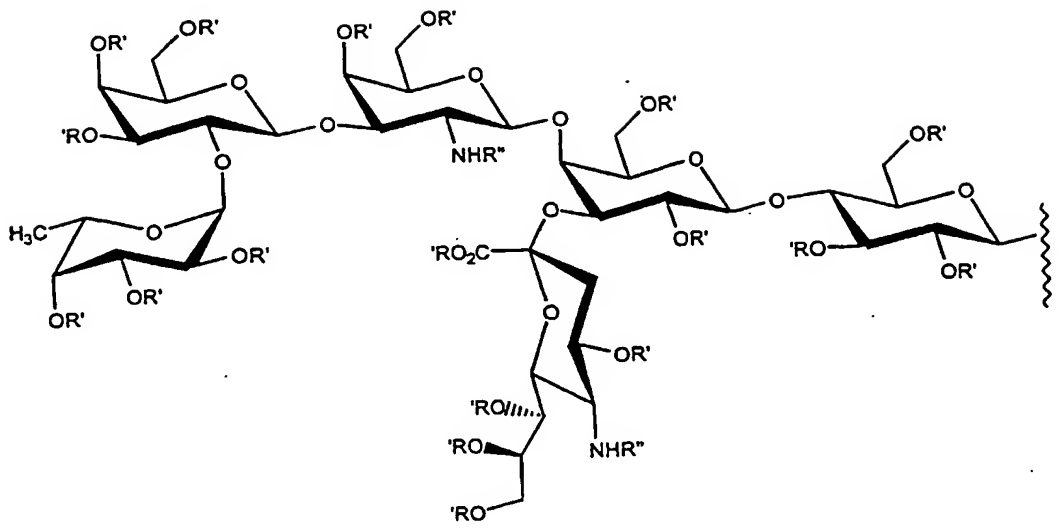
8. The compound of claim 7 wherein n is 3.

9. The compound of claim 7, wherein R' and R" are each hydrogen or a protecting group.

10. The compound of claim 9, wherein R' and R" are each protecting groups independently selected from the group consisting of Fmoc, acetyl, Boc, *t*-butyl and TSE.

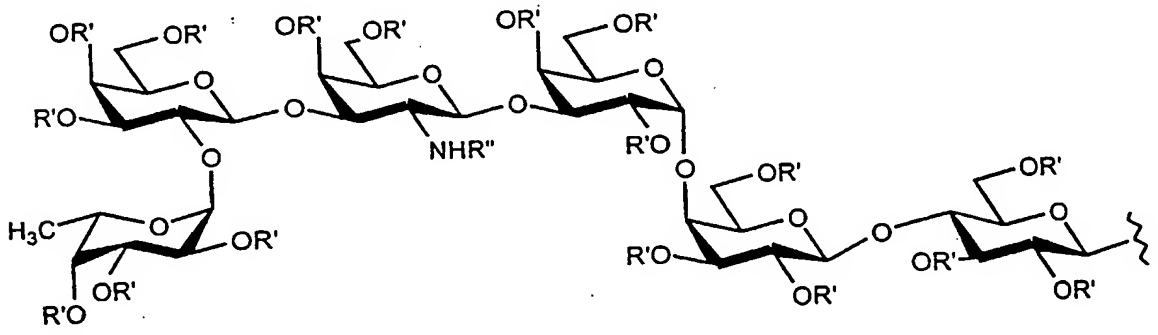
11. The compound of claim 1, 4, 7 or 8, or the glycoconjugate of claim 5 or 6, wherein the carbohydrate determinant is selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, N3,Tn, TF, STN, (2,3)ST, 2,6-STn, and Le^y.

12. The compound or glycoconjugate of claim 11, wherein A is the carbohydrate determinant fucosyl GM1 having the structure:



wherein each occurrence of R' is independently hydrogen or a protecting group; and wherein each occurrence of R" is independently hydrogen or a nitrogen protecting group.

13. The compound or glycoconjugate of claim 11, wherein A is the carbohydrate determinant Globo-H having the structure:



wherein each occurrence of R' is independently hydrogen or a protecting group, and wherein R" is hydrogen or a nitrogen protecting group.

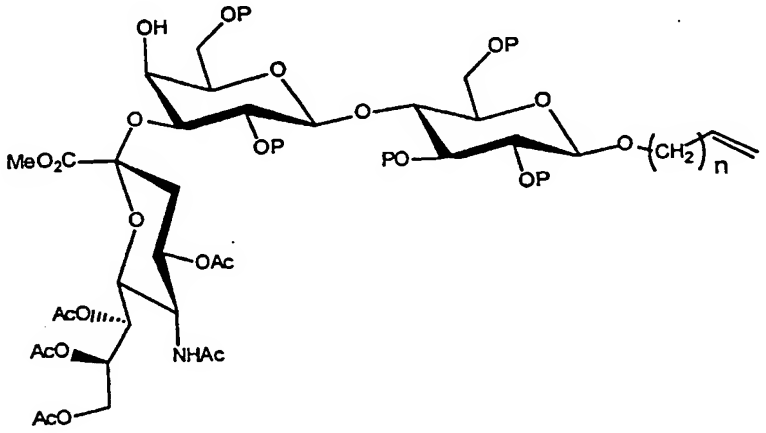
14. A method for the synthesis of complex carbohydrates comprising:

(a) providing a carbohydrate acceptor having a reducing end alkenyl group;

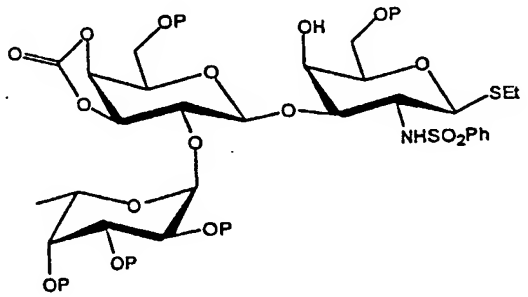
(b) providing a suitable donor compound; and

(c) coupling said donor and acceptor under conditions to generate an alkenyl glycoside.

15. The method of claim 14, wherein the step of providing a carbohydrate acceptor having a reducing end alkenyl group comprises providing an acceptor having the structure:

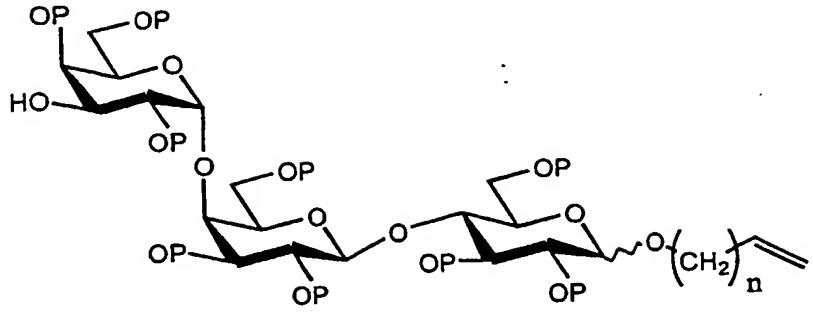


wherein P is a protecting group and n is 0-8, and wherein the step of providing a suitable donor compound comprising providing a donor having the structure:

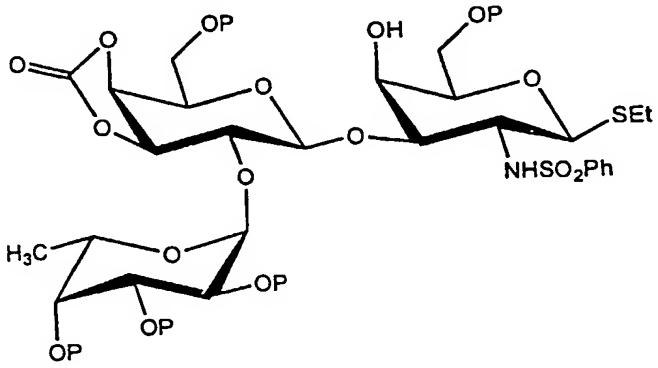


wherein n is 0-8, and wherein P is a protecting group.

16. The method of claim 14, wherein the step of providing a carbohydrate acceptor having a reducing end alkenyl group comprises providing an acceptor having the structure:



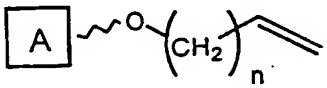
wherein P is a protecting group and n is 0-8, and wherein the step of providing a suitable donor compound comprising providing a donor having the structure:



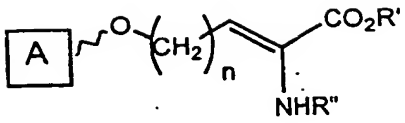
wherein n is 0-8 and P is a protecting group.

17. A method for the synthesis of a glycoamino acid comprising the steps of:

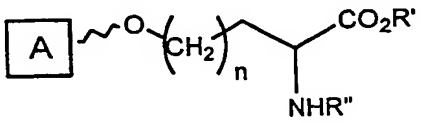
(a) providing an alkenyl glycoside having the structure:



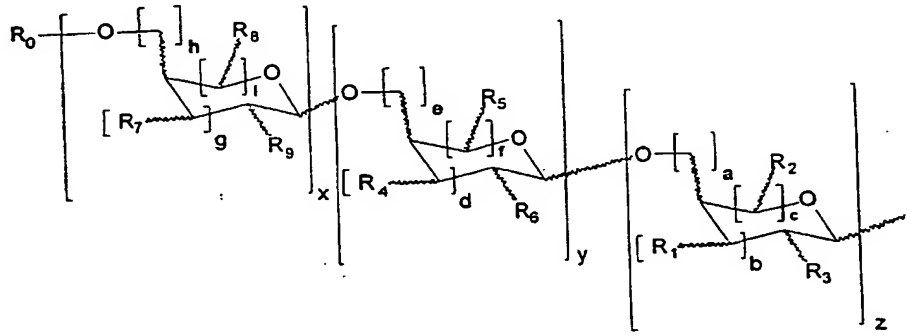
and reacting said alkenyl glycoside under suitable conditions to generate an enamide ester having the structure:



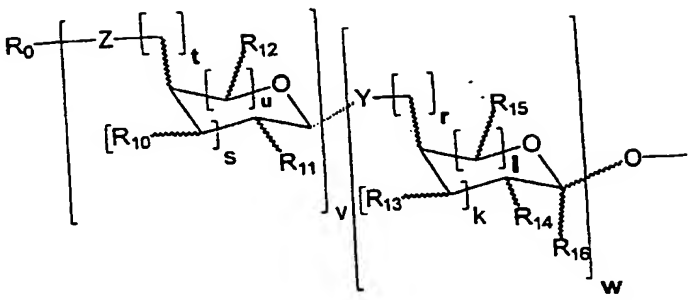
(b) reacting said enamide ester under suitable conditions to generate a glycoamino acid having the structure:



wherein, for each of the structures above, n is 0-8, wherein A is a carbohydrate domain having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein R_1, R_2, R_3, R_4 , R_5, R_6 , R_7, R_8 and R_9 are each independently hydrogen, OH, OR^i, NH_2, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R^i is hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group or a saccharide moiety having the structure:

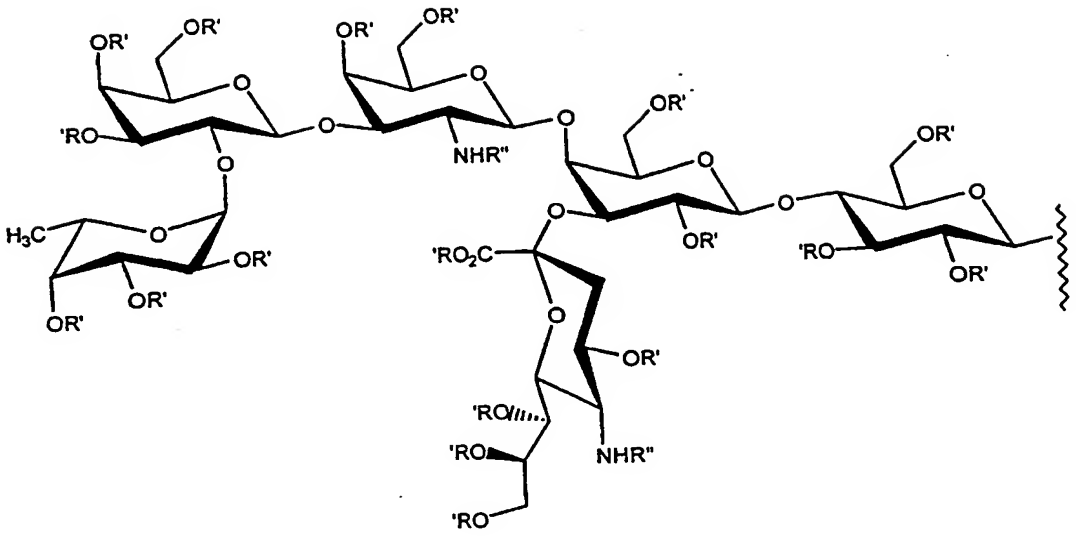


wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; wherein R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, OH, OR^{iii}, NH_2, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group; and wherein R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

and wherein for the glycoamino acid structure R' and R" are each independently protecting group or hydrogen.

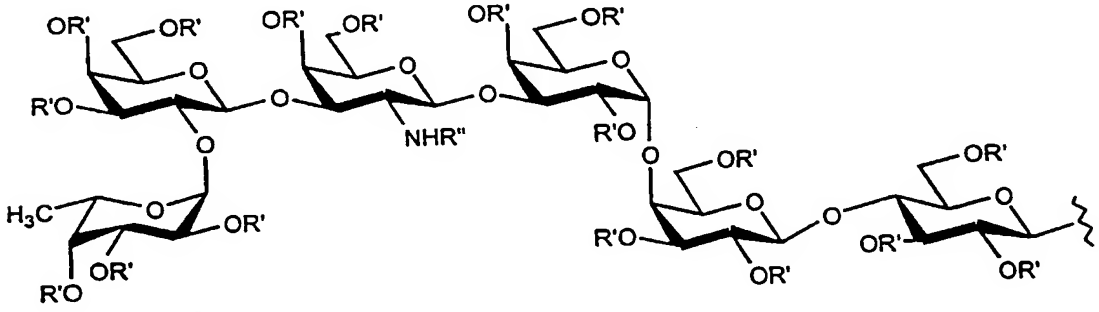
18. The method of claim 17, wherein the carbohydrate determinant is selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, STN, (2,3)ST, Le^y, N3, Tn, 2,6-STn, and TF.

19. The method of claim 18, wherein A is a carbohydrate determinant having the structure:



wherein each occurrence of R' is independently hydrogen or a protecting group; and wherein each occurrence of R" is independently hydrogen or a nitrogen protecting group.

20. The method of claim 18, wherein A is a carbohydrate determinant having the structure:



wherein each occurrence of R' is independently hydrogen or a protecting group, and wherein R" is hydrogen or a nitrogen protecting group.

21. The method of claim 17, wherein the step of reacting an alkenyl glycoside under suitable conditions to generate an enamide ester comprises reacting an alkenyl glycoside

first under oxidative cleavage conditions and second under olefination conditions in the presence of base and phosphonate to generate an enamide ester.

22. The method of claim 21, wherein said oxidative cleavage conditions comprise ozonolysis, and wherein the base is tetramethylguanidine.

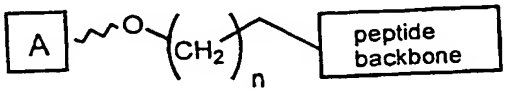
23. The method of claim 21, wherein said oxidative cleavage conditions are OsO_4 and periodate, or OsO_4 and $Pb(OAc)_4$, and wherein the base is lithium t-butoxide or lithium hexamethyl disilylazide.

24. The method of claim 17, wherein the step of reacting said enamide ester under suitable conditions to generate a glycoamino acid comprises reacting said enamide ester under hydrogenation conditions and subsequent reaction under deprotection conditions to generate a glycoamino acid.

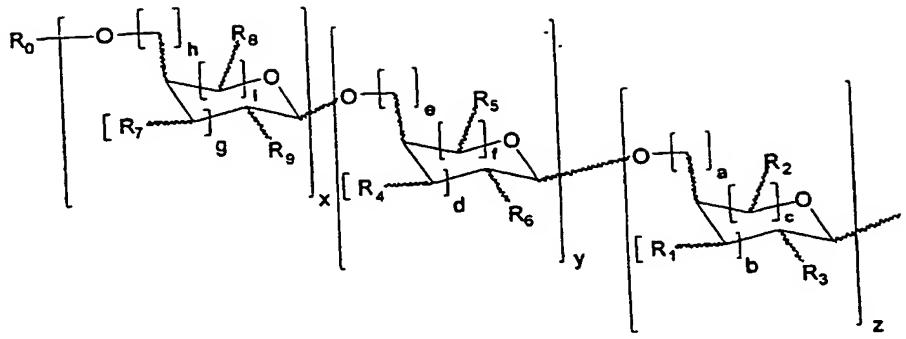
25. The method of claim 24, wherein said hydrogenation is achieved via asymmetric hydrogenation.

26. The method of claim 25, wherein said asymmetric hydrogenation is achieved by utilizing an ethyl DuPHOS catalyst precursor.

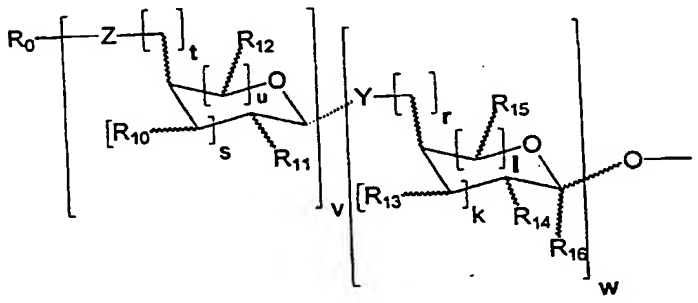
27. A multi-antigenic glycopeptide comprising a peptidic backbone made up of at least three amino acids, wherein one or more of said amino acids are substituted with an n-alkyl glycosidic moiety having the structure:



wherein each occurrence of A is a carbohydrate determinant having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein R_1, R_2, R_3, R_4 , R_5, R_6 , R_7, R_8 and R_9 are each independently hydrogen, OH, OR^i, NH_2, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R^i is hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group or a saccharide moiety having the structure:

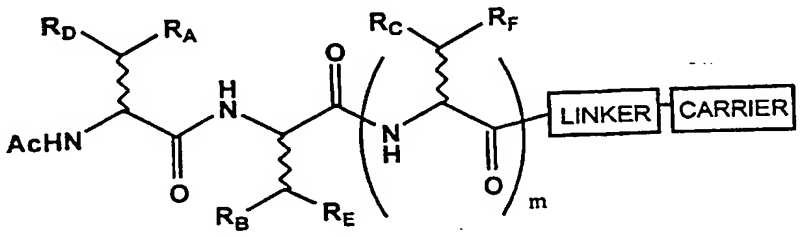


wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; wherein R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, OH, OR^{iii}, NH_2, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched

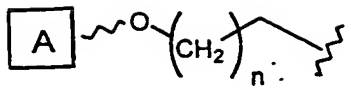
chain alkyl or aryl group; wherein R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group; and wherein R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

wherein each occurrence of n is independently 0-8, whereby, if for each occurrence of n, n = 0, at least one occurrence of A has a different structure from other occurrences of A; and wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid.

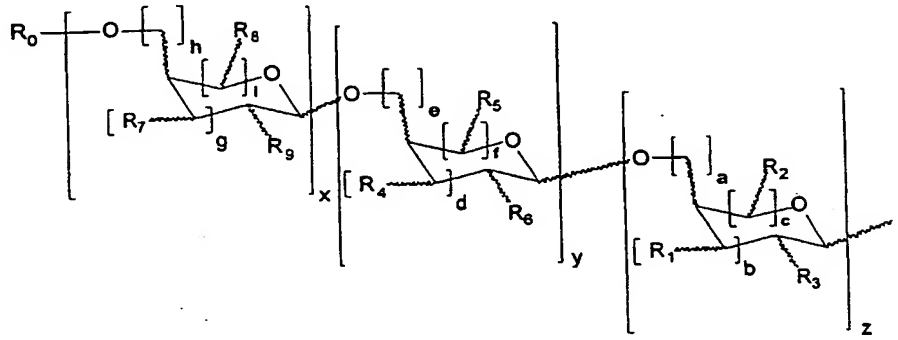
28. The glycopeptide of claim 27, wherein said glycopeptide is a construct having the structure:



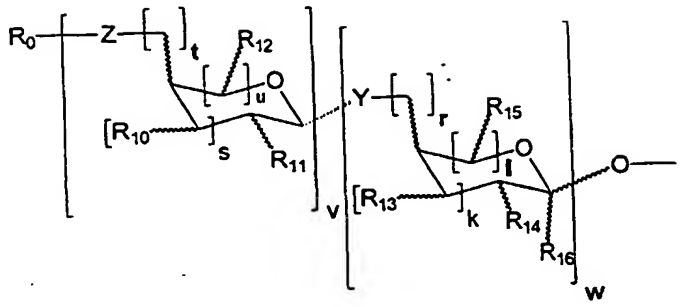
wherein the linker is either a free carboxylic acid, (carboxamido)alkyl carboxamide, MBS, primary carboxamide, mono- or dialkyl carboxamide, mono- or diarylcarboxamide, linear or branched chain (carboxy)alkyl carboxamide, linear or branched chain (alkoxycarbonyl)alkyl-carboxamide, linear or branched chain (carboxy)arylalkylcarboxamide, linear or branched chain (alkoxycarbonyl)alkylcarboxamide, an oligoester fragment comprising from 2 to about 20 hydroxy acyl residues, a peptidic fragment comprising from 2 to about 20 amino acyl residues, or a linear or branched chain alkyl or aryl carboxylic ester; wherein the carrier is a protein or lipid; wherein m is 1, 2 or 3; wherein R_A, R_B and R_C are each independently H or methyl; and wherein R_D, R_E and R_F are each independently an alkyl glycosidic moiety having the structure:



wherein each occurrence of A is independently selected from a carbohydrate domain having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that x, y and z are not simultaneously 0; wherein the carbohydrate domain is linked to the respective amino acyl or hydroxy acyl residue by substitution of a side group substituent selected from the group consisting of OH, COOH and NH_2; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein R_1, R_2, R_3, R_4 , R_5, R_6 , R_7, R_8 and R_9 are each independently hydrogen, OH, OR^i, NH_2, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R^i is hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group or a saccharide moiety having the structure:



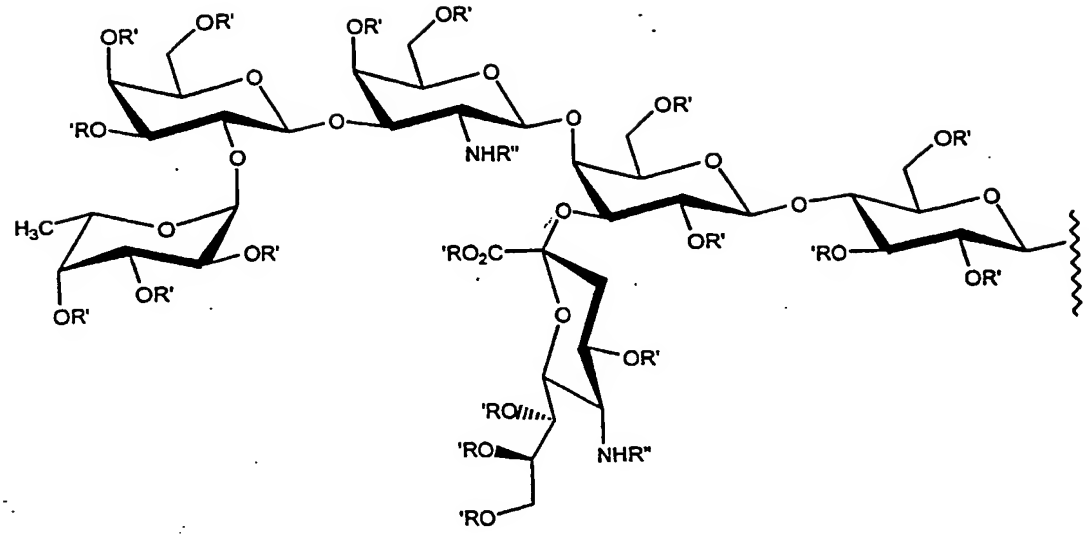
wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; wherein R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, OH, OR^{iii}, NH_2, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group; and wherein R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group; and

wherein each occurrence of n is independently 0-8, whereby, if for each occurrence of n, n = 0, at least one occurrence of A has a different structure from other occurrences of A; and wherein the n-alkyl glycosidic moiety is either α- or β-linked to an amino acid.

29. The compound of claim 27 or the construct of 28 , wherein each occurrence of A is independently Globo-H, fucosyl GM1, KH-1, glycophorin, Le^y, N3, Tn, 2,6-STn, (2,3)ST, or TF.

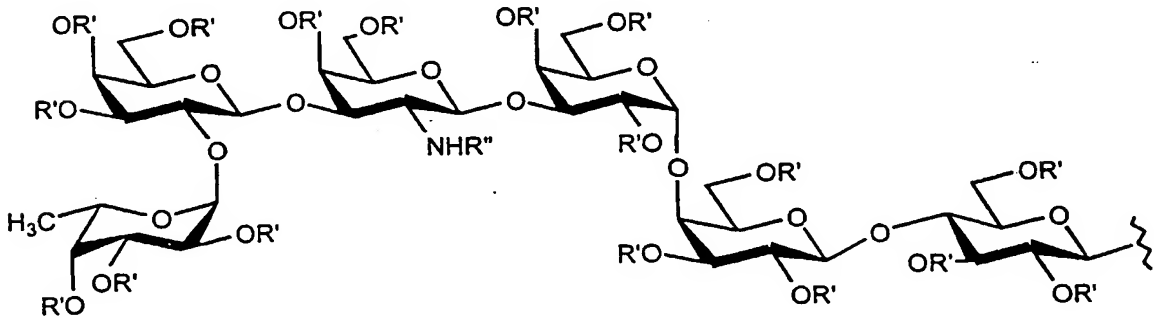
30. The construct of claim 28, wherein said compound has three occurrences of A comprising Tn, Globo-H and Le^y

31. The compound of claim 27 or the construct of claim 28, wherein at least one occurrence of A is a carbohydrate determinant having the structure:



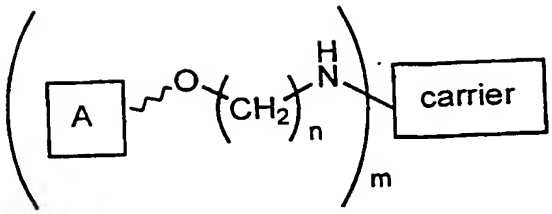
wherein each occurrence of R' is independently hydrogen or a protecting group; and wherein each occurrence of R" is independently hydrogen or a nitrogen protecting group.

32. The compound of claim 27 or the construct of claim 28, wherein at least one occurrence of A is a carbohydrate determinant having the structure:

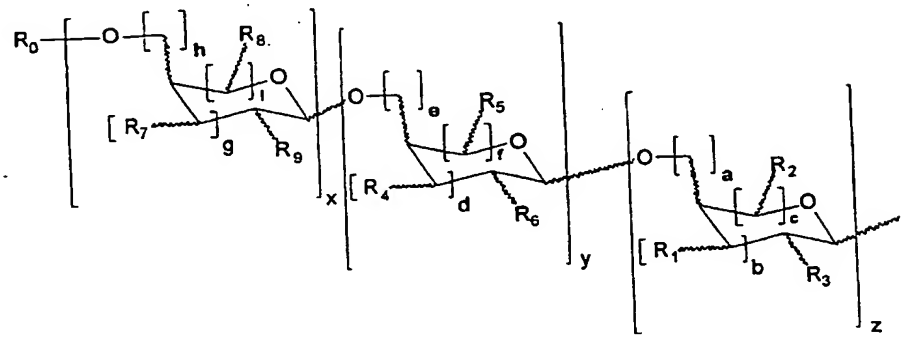


wherein each occurrence of R' is independently hydrogen or a protecting group; and wherein R" is hydrogen or a nitrogen protecting group.

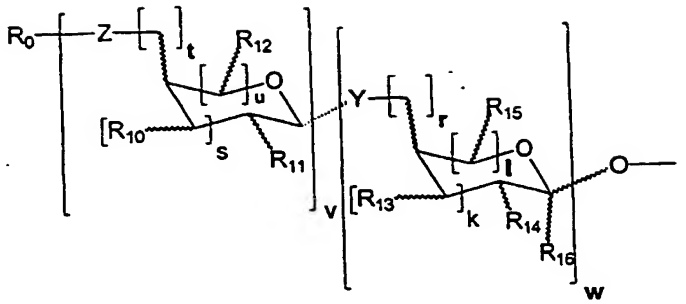
33. A synthetic construct having the structure:



wherein A is a carbohydrate domain having the structure:



wherein a, b, c, d, e, f, g, h, i, x, y and z are independently 0, 1, 2 or 3, with the proviso that x, y and z are not simultaneously 0; wherein R_0 is hydrogen, a linear or branched chain alkyl, acyl, arylalkyl or aryl group; wherein R_1, R_2, R_3, R_4 , R_5, R_6 , R_7, R_8 and R_9 are each independently hydrogen, OH, OR^i, NH_2, $NHCOR^i$, F, CH_2OH, CH_2OR^i, a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R^i is hydrogen, CHO, $COOR^{ii}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group or a saccharide moiety having the structure:



wherein Y and Z are independently NH or O; wherein k, l, r, s, t, u, v and w are each independently 0, 1 or 2; wherein R_{10}, R_{11}, R_{12}, R_{13}, R_{14} and R_{15} are each independently hydrogen, OH, OR^{iii}, NH_2, $NHCOR^{iii}$, F, CH_2OH, CH_2OR^{iii}, or a substituted or unsubstituted linear or branched chain alkyl, (mono-, di- or tri)hydroxyalkyl, (mono-, di- or tri)acyloxyalkyl, arylalkyl or aryl group; wherein R_{16} is hydrogen, COOH, $COOR^{ii}$, $CONHR^{ii}$, a substituted or unsubstituted linear or branched chain alkyl or aryl group; wherein R^{iii} is hydrogen, CHO, $COOR^{iv}$, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group; and wherein R^{ii} and R^{iv} are each independently H, or a substituted or unsubstituted linear or branched chain alkyl, arylalkyl or aryl group;

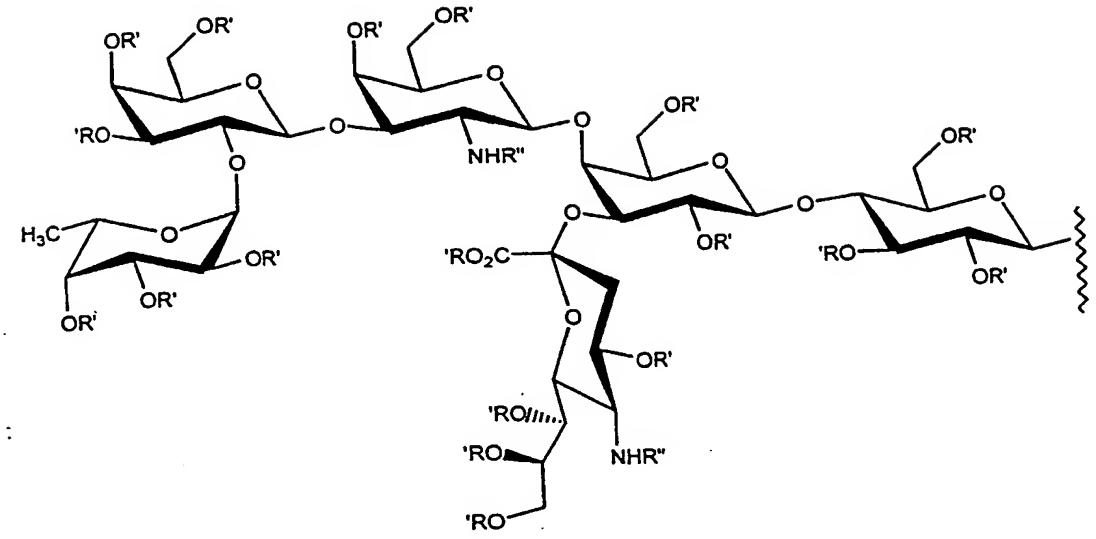
wherein n is 0-8; wherein the carrier a lipid or protein linked directly or through a crosslinker; and wherein m is in the range of 20 to 600.

34. The construct of claim 33, wherein m is in the range of 200 to 600.

35. The construct of claim 33, wherein n is 4.

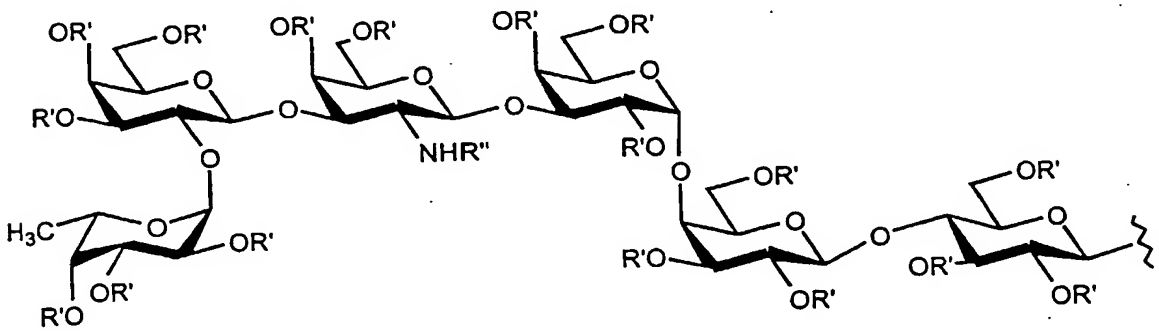
36. The construct of claim 33, wherein the carbohydrate determinant is selected from the group consisting of Globo-H, fucosyl GM1, KH-1, glycophorin, STN, (2,3)ST, 2,6-STn, N3, Tn, TF and Le^y.

37. The construct of claim 33 or 35, wherein A is a carbohydrate determinant, having the structure:



wherein each occurrence of R' is independently hydrogen or a protecting group; and wherein each occurrence of R" is independently hydrogen or a nitrogen protecting group.

38. The construct of claim 33 or 35, wherein A is a carbohydrate determinant, having the structure:



wherein each occurrence of R' is independently hydrogen or a protecting group; and wherein R" is hydrogen or a nitrogen protecting group.

39. A pharmaceutical composition comprising:
a compound or construct of claim 1 or 27, and
a pharmaceutically suitable carrier.

40. A method of treating cancer in a subject suffering therefrom comprising:
administering to a subject a therapeutically effective amount of a compound or construct of claim 1 or 27,
and a pharmaceutically suitable carrier.

41. The method of claim 40, wherein said method comprises preventing the recurrence of cancer in a subject.

42. The method of claim 40 or 41, further comprising co-administering one or more immunological adjuvants.

43. The method of claim 42, wherein at least one of said one or more immunological adjuvants is a saponin adjuvant.

44. The method of claim 43, wherein said saponin adjuvant is GPI-0100.

45. The method of claim 42, wherein at least one of said one or more immunological adjuvants is bacteria or liposomes.

46. The method of claim 45, wherein the immunological adjuvant is Salmonella minnesota cells, bacille Calmette-Guerin or QS21.

47. The method of claim 40 or 41, wherein the cancer is a solid tumor.

48. The method of claim 40 or 41, wherein the subject is in clinical remission, or where the subject has been treated by surgery, has limited unresected disease.

49. A method of inducing antibodies in a subject, wherein the antibodies are capable of specifically binding with tumor cells, which comprises administering to the subject an amount of a compound or construct of claim 1 or 27 effective to induce the antibodies.

50. The method of claim 49, further comprising co-administering one or more immunological adjuvants.

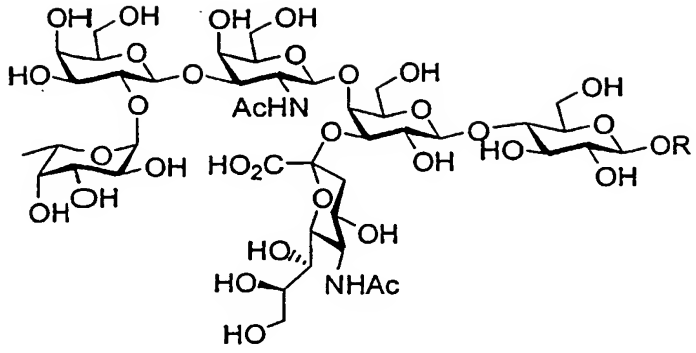
51. The method of claim 50, wherein at least one of said one or more immunological adjuvants is a saponin adjuvant.

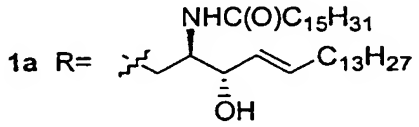
52. The method of claim 51, wherein said saponin adjuvant is GPI-0100.

53. The method of claim 49, wherein at least one of said one or more immunological adjuvants is bacteria or liposomes.

54. The method of claim 53, wherein the immunological adjuvant is *Salmonella minnesota* cells, bacille Calmette-Guerin or QS21.

55. The method of claim 49, wherein the subject is in clinical remission, or where the subject has been treated by surgery, has limited unresected disease.

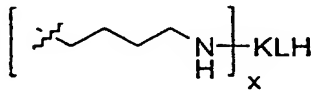




1a R=

1b R=

1c R=



1d R=

x = 20-600

Figure 1

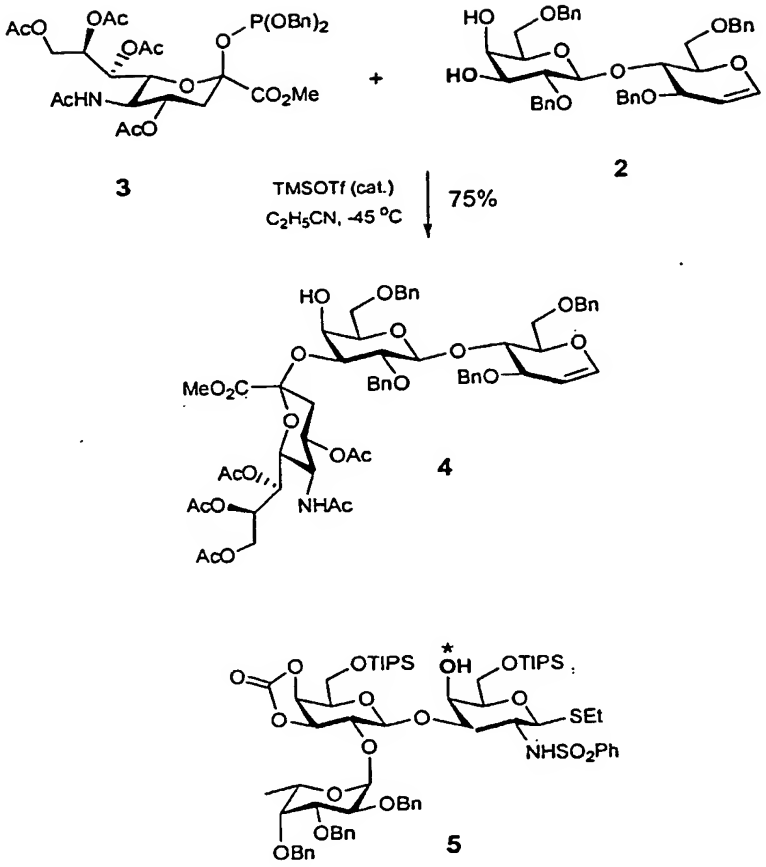

AcO
OAc
OAc
AcHN
AcO
P(OBn)2
CO2Me
3
+
HO
OBn
HO
BnO
OBn
BnO
2
TMSOTf (cat.)
C2H5CN, -45 °C
75%
HO
OBn
OBn
MeO2C
BnO
BnO
OAc
AcO
AcO
NHAc
AcO
4
OTIPS
OH
OTIPS
SEt
NHSO2Ph
OBn
OBn
OBn
5

Figure 2

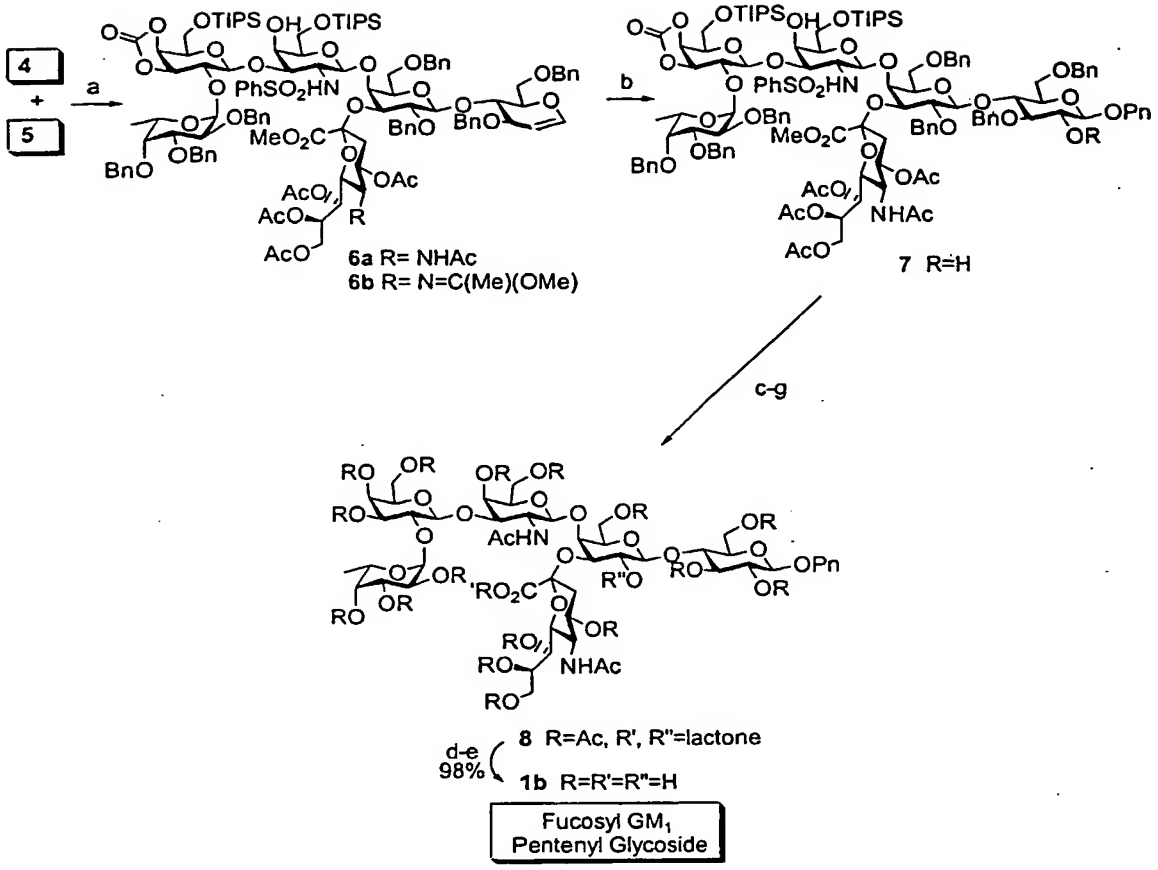

4
+
5
a
OTIPS
OH
OTIPS
OBn
PhSO2HN
MeO2C
BnO
AcO
OAc
R
6a R= NHAc
6b R= N=C(Me)(OMe)
b
OPn
NHAc
7 R=H
c-g
RO
OR
AcHN
R"O
RO2C
8 R=Ac, R', R"=lactone
d-e
98%
1b R=R'=R"=H
Fucosyl GM1
Pentenyl Glycoside

Figure 3

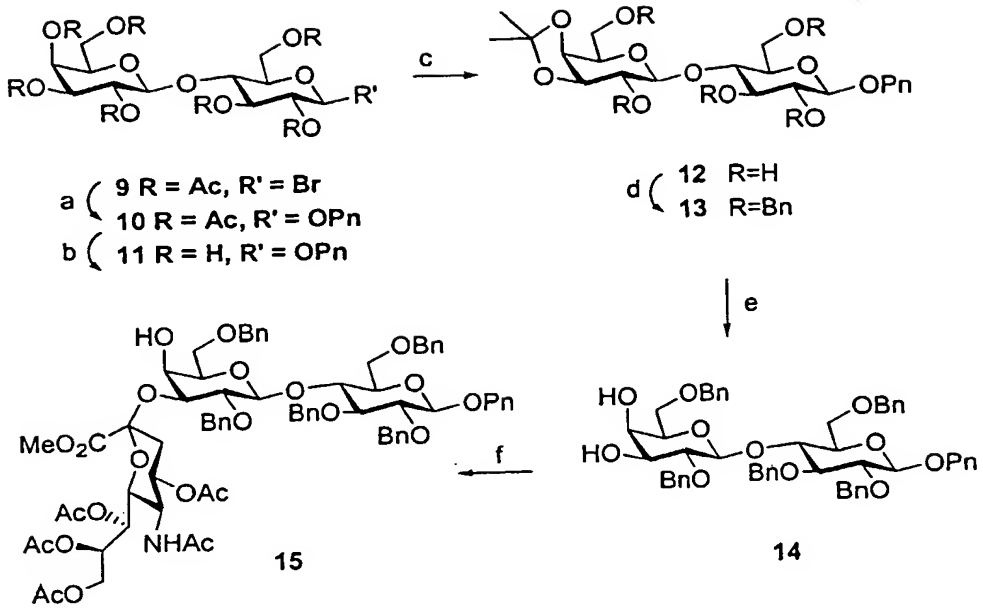


Figure 4

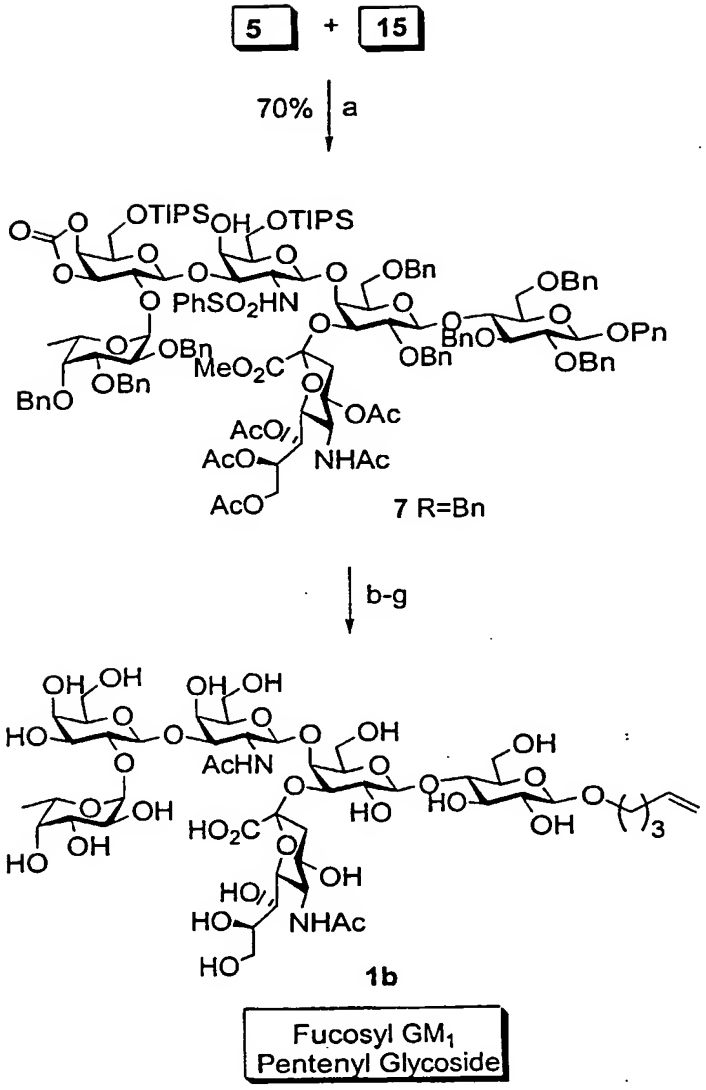

5
+
15
70%
a
OTIPS
OH
OTIPS
PhSO2HN
OBn
OPn
MeO2C
OAc
AcO
NHAc
7 R=Bn
b-g
AcHN
HO2C
1b
Fucosyl GM1
Pentenyl Glycoside

Figure 5

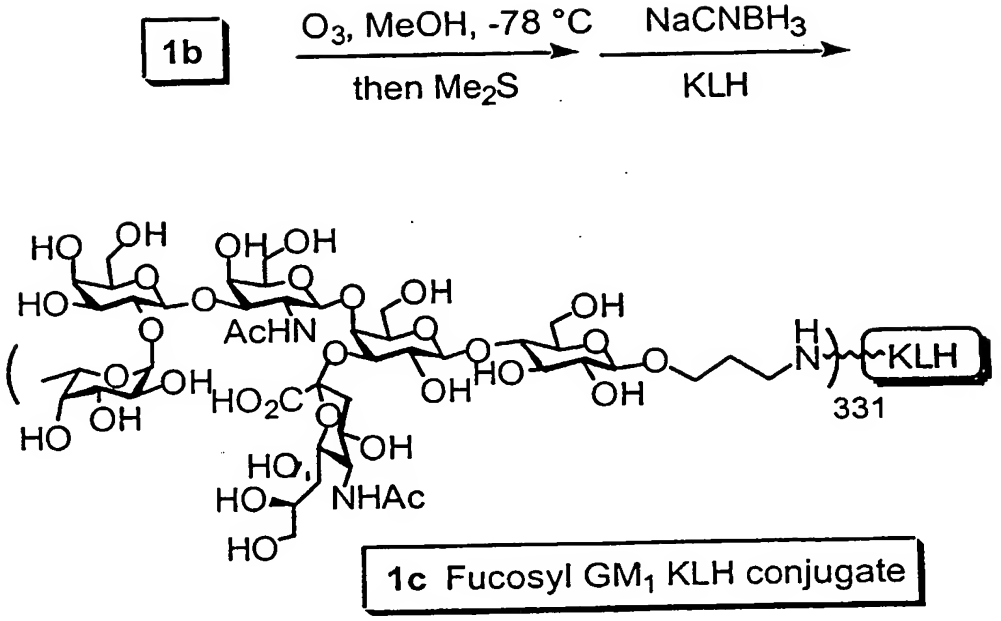
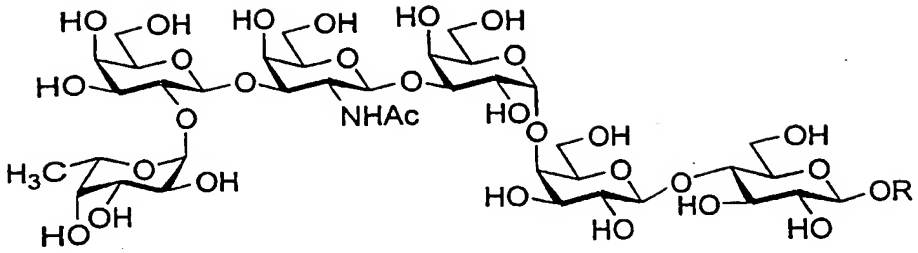
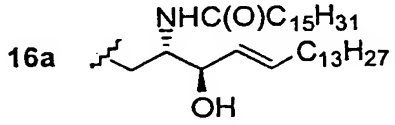
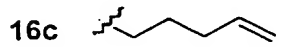
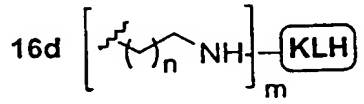

1b
O3, MeOH, -78 °C
then Me2S
NaCNBH3
KLH
HO
OH
AcHN
HO2C
NHAc
331
KLH
1c Fucosyl GM1 KLH conjugate

Figure 6



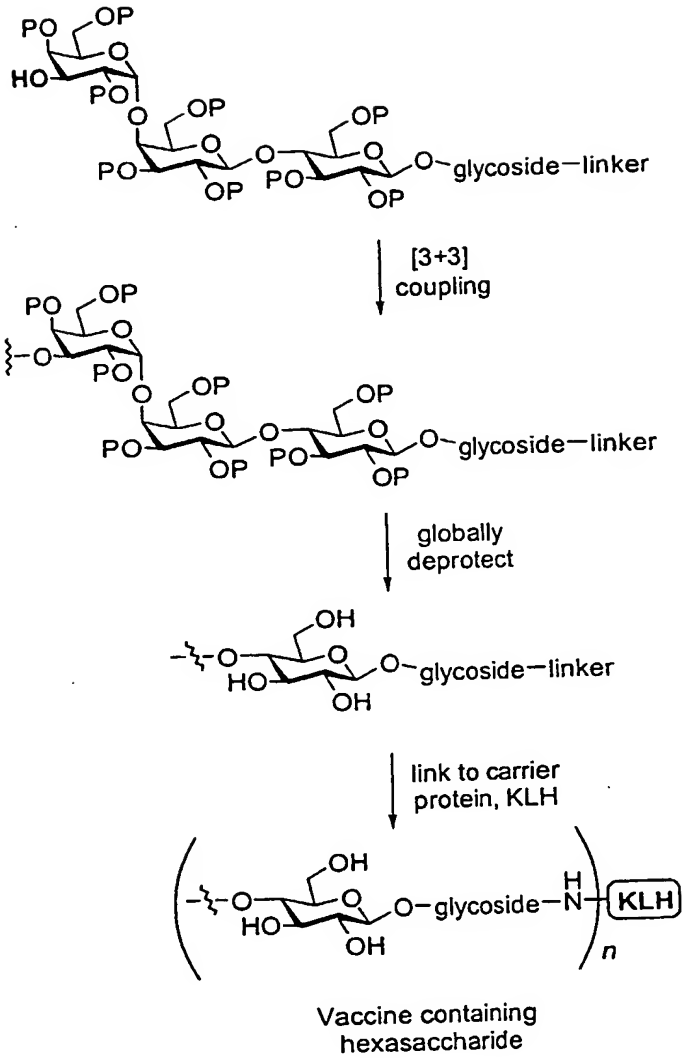






m = 20-600

Figure 7



Vaccine containing
hexasaccharide

n = 20-600

Figure 8

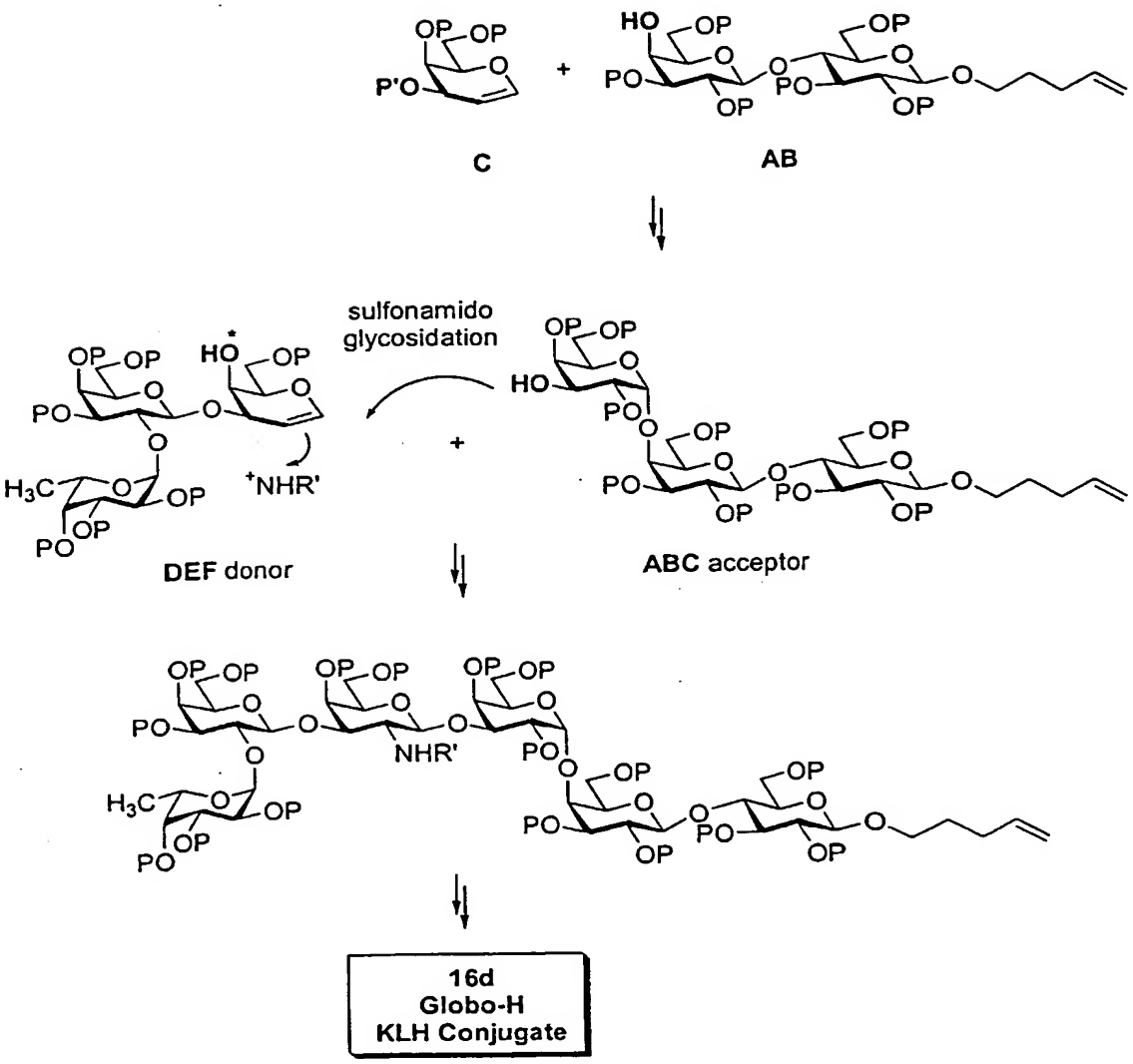

C
AB
sulfonamido glycosidation
DEF donor
ABC acceptor
16d
Globo-H
KLH Conjugate

Figure 9

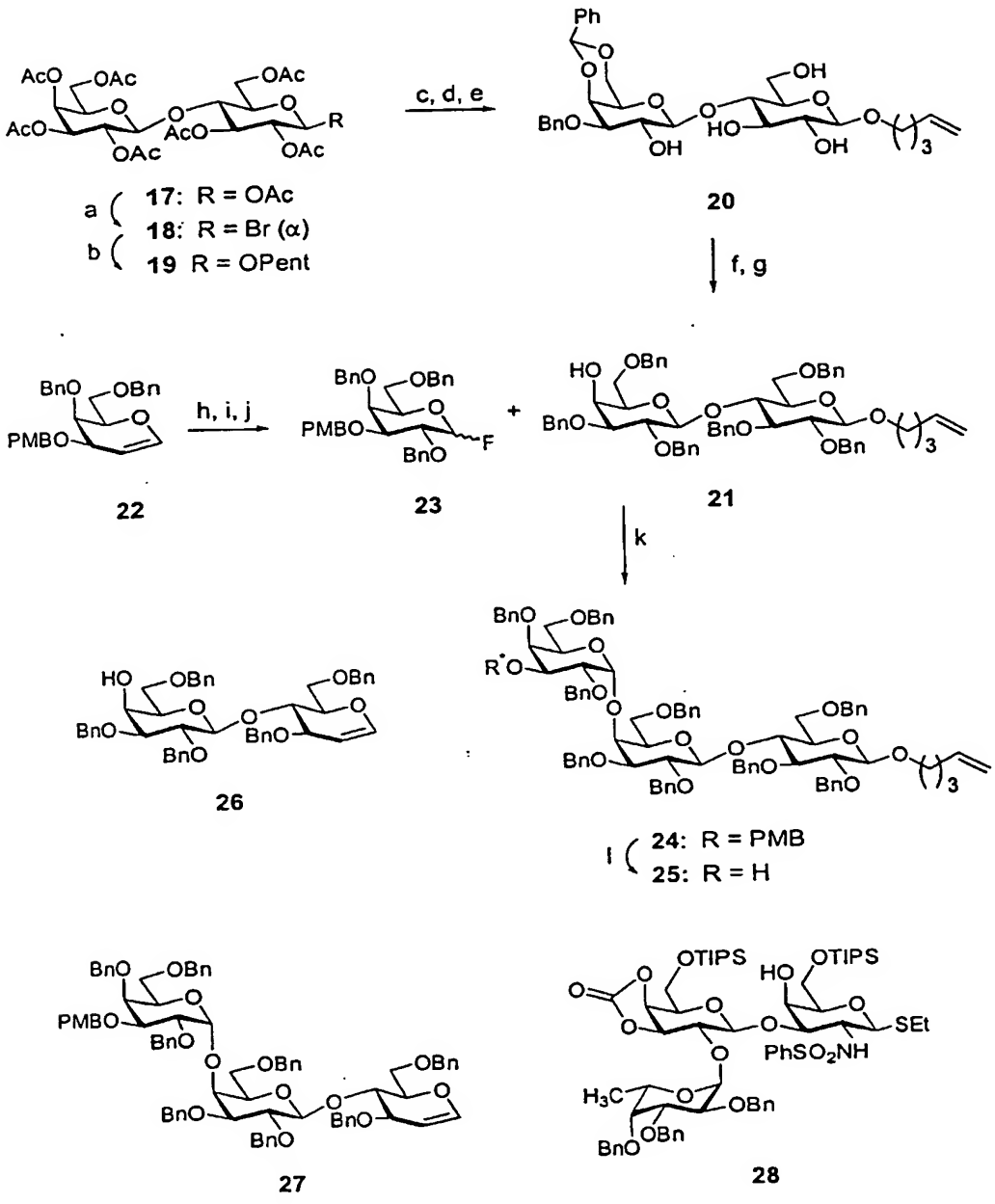

c, d, e
a
b
17: R = OAc
18: R = Br (α)
19 R = OPent
20
f, g
h, i, j
22
23
21
k
26
l
24: R = PMB
25: R = H
27
28

Figure 10

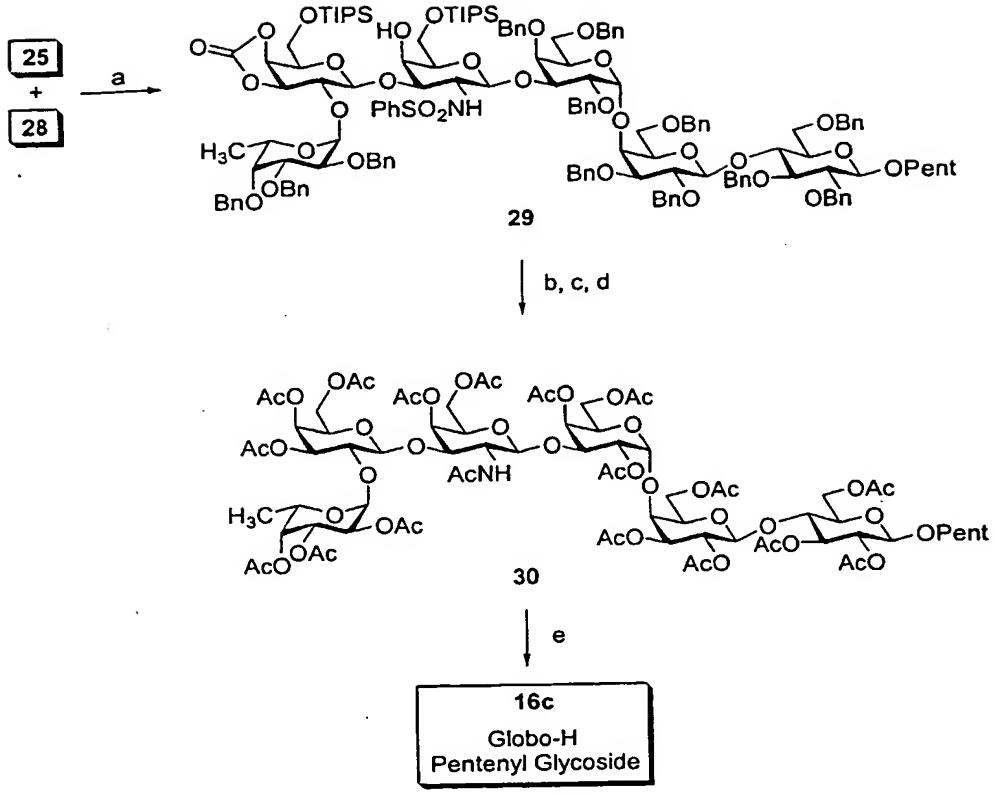

25
+
28
a
OTIPS
HO
OTIPS
BnO
OBn
PhSO2NH
H3C
OBn
BnO
OBn
BnO
OBn
BnO
OBn
BnO
OPent
OBn
29
b, c, d
AcO
OAc
AcNH
H3C
OAc
OPent
30
e
16c
Globo-H
Pentenyl Glycoside

Figure 11

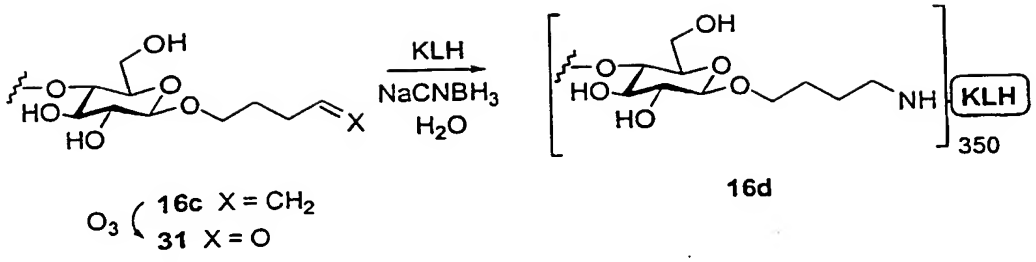


Figure 12

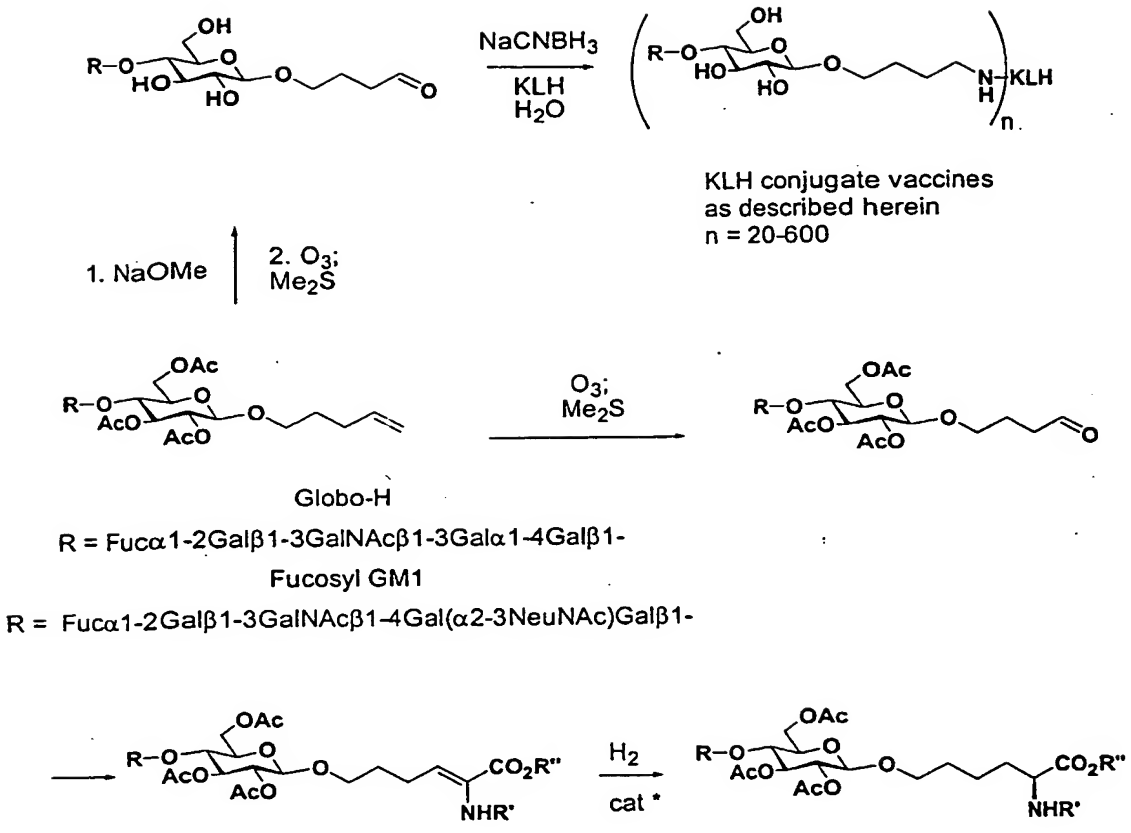

NaCNBH3
KLH
H2O
KLH conjugate vaccines
as described herein
n = 20-600
1. NaOMe
2. O3;
Me2S
O3;
Me2S
Globo-H
R = Fucα1-2Galβ1-3GalNAcβ1-3Galα1-4Galβ1-
Fucosyl GM1
R = Fucα1-2Galβ1-3GalNAcβ1-4Gal(α2-3NeuNAc)Galβ1-
H2
cat *

Figure 13

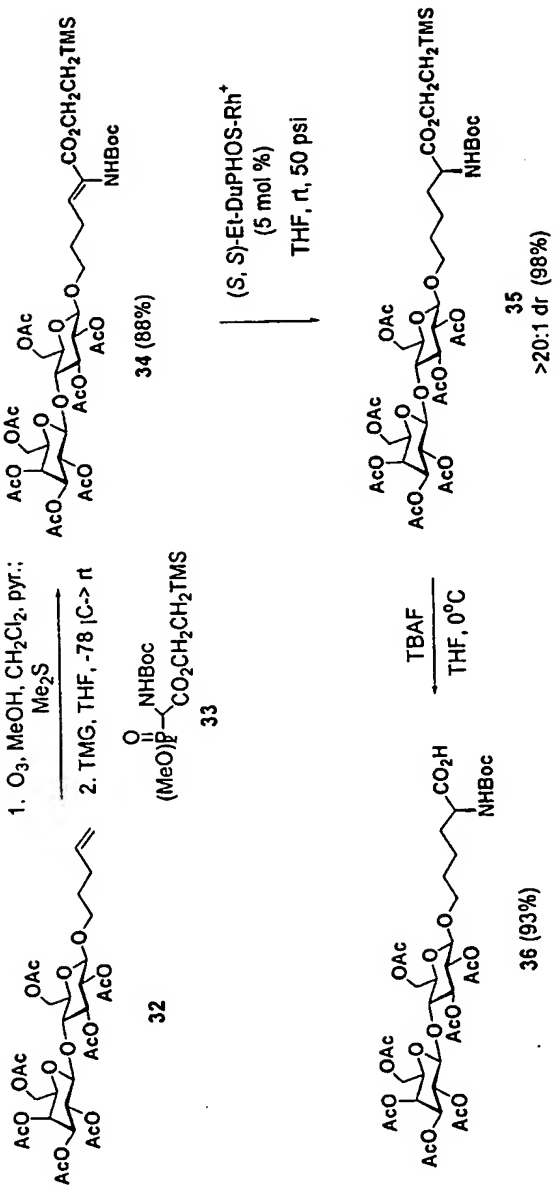

1. O_3, MeOH, CH_2Cl_2, pyr.; Me_2S
2. TMG, THF, -78 °C-> rt
32
33
34 (88%)
(S, S)-Et-DuPHOS-Rh+
(5 mol %)
THF, rt, 50 psi
35
>20:1 dr (98%)
TBAF
THF, 0°C
36 (93%)

Figure 14

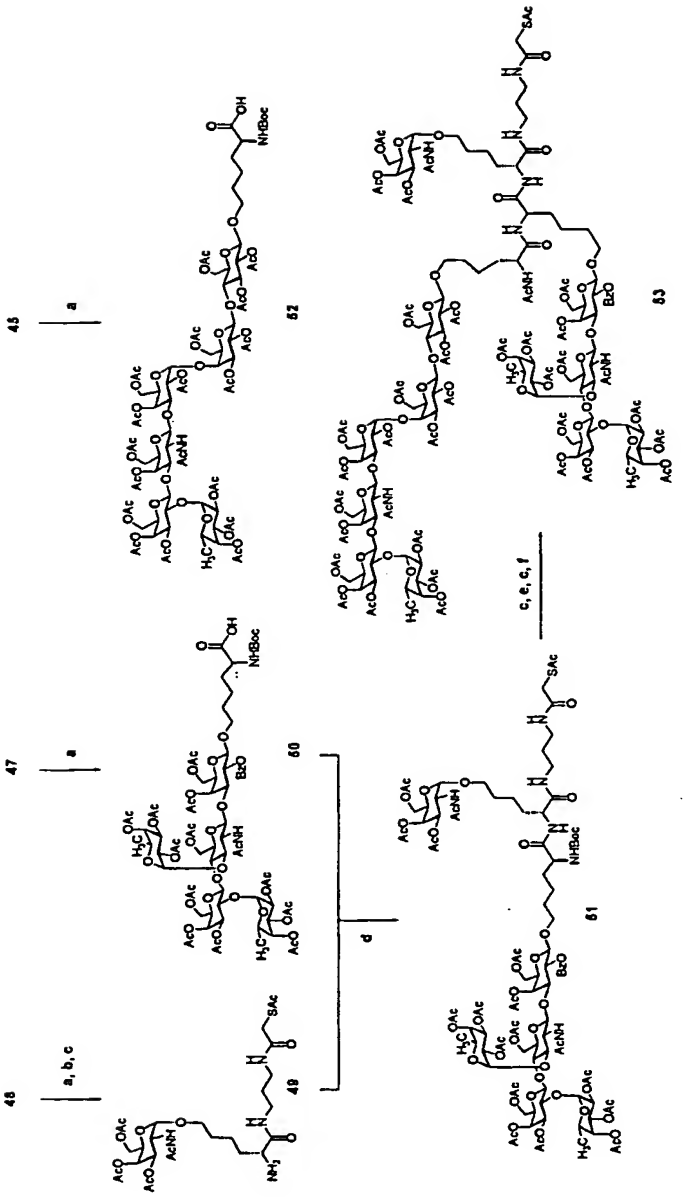


Figure 15

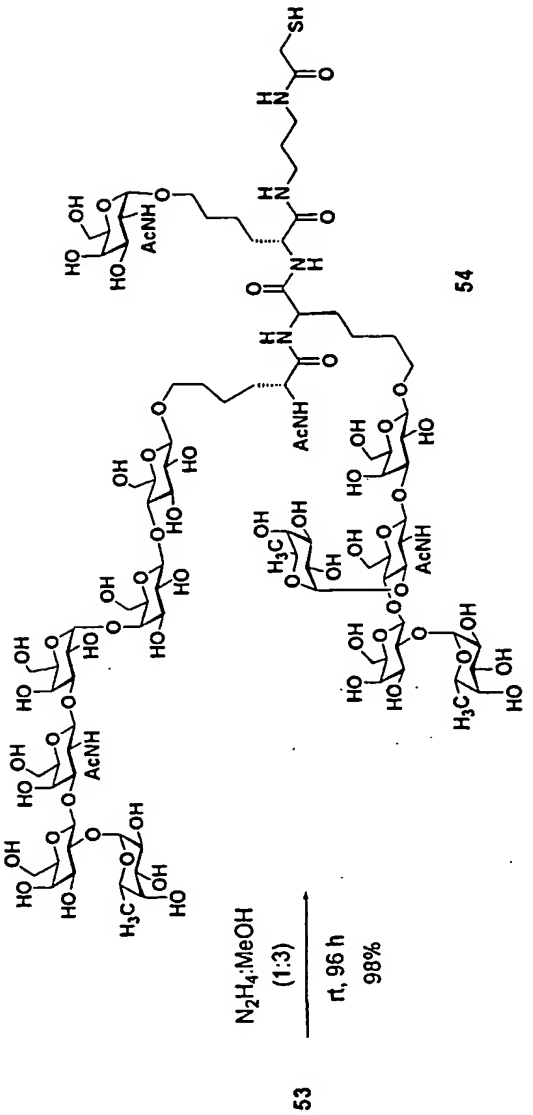


Figure 16

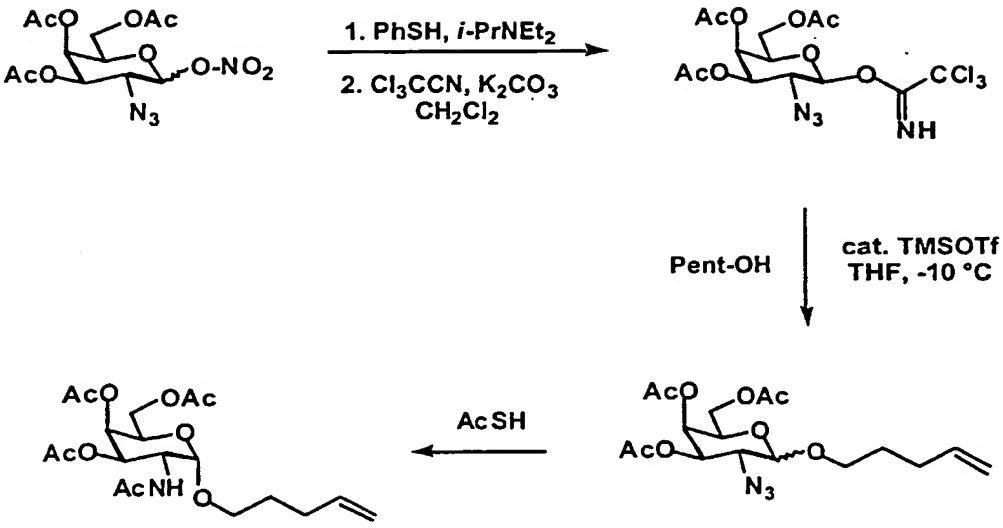

AcO
OAc
AcO
O-NO2
N3
1. PhSH, i-PrNEt2
2. Cl3CCN, K2CO3
CH2Cl2
AcO
OAc
AcO
CCl3
N3
NH
Pent-OH
cat. TMSOTf
THF, -10 °C
AcO
OAc
AcO
N3
AcSH
AcO
OAc
AcO
AcNH

Figure 17